IN THE SPECIFICATION

Please amend the specification as follows:

Please amend the paragraph beginning on page 19, line 19 as follows:

Figure 2. *In vivo* enhancement of rAAV transduction with DOXIL® [[Doxil]]. Male Balb/c mice intravenously administered DOXIL® [[Doxil]] were endotracheally instilled with 1 x 10^{11} DRP AAV2FLAG-Luc (01:004). A) Effect on rAAV lung transduction. B) Effect on rAAV tracheal and bronchial transduction.

Please amend the paragraph beginning on page 19, line 26 as follows:

Figure 4. Luciferase activity in HeLa cells after infection with A) AV2.RSVLuc or AV2.RSVlucCap5 (100 or 1000 ppc) or B) AV2CMVluc or AV2CMVluc Cap5 (500 ppc), and ~~co-administration of~~ LLnL (~~40, 200 or 400~~ μM), Z-LLL (4 μM), or doxorubicin (0.5[[,]] or 1.0 [[or 5.0]] μM) ~~or a combination of LLnL (4, 10, 20 or 200 μM) and doxorubicin (0.5, 1.0 or 5.0 μM)~~. C) Comparison of CMV and RSV promoters in AAV-2 vectors in HeLa cells.

Please amend the paragraph beginning on page 20, line 6 as follows:

Figure 6. Luciferase activity in ferret fibroblasts after infection with AV2CMVluc or AV2CMVluc Cap5 (500 ppc), and co-administration of LLnL (40, 200 or 400 μM), Z-LLL (4 μM), or doxorubicin (1 μM). A) Comparison of AV2CMVluc and AV2CMVlucCap5. B) RLU at 1 and 5 days for AV2CMVluc (left panel) and AV2CMVlucCap5 (right panel) in ferret fibroblasts.

Please amend the paragraph beginning on page 20, line 13 as follows:

Figure 8. Luciferase activity in polarized airway epithelial cells at 3 days (A) and 15 days (B) after apical infection with 5 x 10^9 AV2RSVLuc or AV2RSVlucCap5 and co-administration of LLnL (40 μM) or doxorubicin (1.0 or 5.0 μM) or a combination of LLnL (40 μM) and doxorubicin (1.0 or 5.0 μM). The panel in the upper right summarizes RLU on days 3 and 15.

Please amend the paragraph beginning on page 20, line 17 as follows:

Figure 9. Luciferase activity in C57Bl6 mouse lung (upper panel) or trachea and bronchi (lower panel) at 2 weeks (A) or C57Bl6 mouse lung (upper panel) or trachea and bronchi (lower panel) at 6 weeks (B) after infection (via nasal aspiration) with AV2RSVlucCap5 (3 times with 10 μl of 2 x 10^9 particles/μl in 40 μl, for a total of 6 x 10^{10} particles) and co-administration of Z-LLL (200 μM), doxorubicin (200 μM), or a combination of Z-LLL (200 μM) and doxorubicin (200 μM). For each group, n = 12. Lung and trachea with some bronchial tissue was isolated and, after extraction, luciferase activity/total protein in the tissue extraction determined.

Please amend the paragraph beginning on page 20, line 24 as follows:

Figure 10. Luciferase activity in mouse lung (A) or trachea and bronchi (B) at 2 weeks, 6 weeks or 3 months after infection with AV2RSVlucCap5 and co-administration of Z-LLL (200 μM), doxorubicin (200 μM) or a combination of Z-LLL (200 μM) and doxorubicin (200 μM). The luciferase assay was performed at 80% sensitivity. Lung and trachea with some bronchial tissue was isolated and, after extraction, luciferase activity/total protein in the tissue extraction determined.

Please amend the paragraph beginning on page 20, line 30 as follows:

Figure 11. The effects of proteasome inhibitors LLnL (left panel) and Doxorubicin (Dox)

(right panel) on AV2Luc and AV2/5Luc transduction of immortalized human airway cell lines IB3 (panel A) and A549 (panel B) were evaluated. Proteasome-modulating agents were co-administered with each rAAV vector (MOI of 500 particles per cell) at the time of infection and transduction was evaluated 24 hours later. Various concentrations of each chemical were evaluated as indicated in each graph. Data represent the mean (+/-SEM) relative luciferase activity experiment (N=4).

Please amend the paragraph beginning on page 21, line 18 as follows:

Figure 13. Dox and LLnL provide additive induction of rAV2 transduction. Hela cells (A) ~~(left panel)~~ and A549 cells (B) ~~(right panel)~~ were infected with rAAV (MOI 500 particles/cell) in the presence of the indicated drug combinations and the expressed transgene was assessed at 24 hours post-infection (Mean +/-SEM, N = 4). Fold induction relative to vehicle-treated rAAV-infected cells is indicated above each bar.

Please amend the paragraph beginning on page 54, line 17 as follows:

These formulations can contain pharmaceutically acceptable vehicles and adjuvants which are well known in the prior art. It is possible, for example, to prepare solutions using one or more organic solvent(s) that is/are acceptable from the physiological standpoint, chosen, in addition to water, from solvents such as acetone, ethanol, isopropyl alcohol, glycol ethers such as the products sold under the name DOWANOL® ~~"Dowanol"~~, polyglycols and polyethylene glycols, C_1-C_4 alkyl esters of short-chain acids, preferably ethyl or isopropyl lactate, fatty acid triglycerides such as the products marketed under the name "Miglyol", isopropyl myristate, animal, mineral and vegetable oils and polysiloxanes.

Please amend the paragraph beginning on page 79, line 12 as follows:

B. HeLa cells were selected to screen for additional agents that enhance rAAV transduction, although any cell strain or line; or primary cells, may be employed. Agents were selected from various classes, such as anti-inflammatories (e.g., dexamethasone and cyclosporin A), NSAIDs

(e.g., ibuprofen), β-adrenergics (e.g., albuterol), antibiotics (e.g., ciprofloxacin, colison, gentamycin, tobramycin, and epoxomycin), lipid lowering agents (e.g., lovastatin, simvastatin and eicosapentaenoic acid), food additives (e.g., tannic acid), viral protease inhibitors (e.g., NORVIR®, KALETRA® and VIRACEPT ~~Norvir, Kaletra, and Viracept~~), chemotherapeutics (e.g., aclacinomycin A, doxorubicin, doxil, camptothecin, taxol and cisplatin) and protease inhibitors (e.g., chymostatin, bestatin and chloroquine). The range of concentrations of the agents to be tested were selected based on solubility profiles, toxicity profiles and/or concentrations previously employed *in vivo*.

Please amend the paragraph beginning on page 80, line 14 as follows:

It should be noted with respect to simvstatin and the lovastatin, that these drugs are formulated as prodrugs and conversion to the activated open ring forms was not confirmed which may have contribute to the negative results. Similarly, the liposomal formulation of doxorubicin, DOXIL® [[doxil]] could not be confirmed to be bioavailable to cell culture cells. Thus, agents which initially screened as statistically negative may be reflective of formulations that are not readily bioavailable to cell culture cells or may be reflective of the limited dose range or exposure time.

Please amend the paragraph beginning on page 81, line 28 as follows:

D. Endotracheal administration of 10^{11} AV2FLAG-luc rAAV particles to male Balb/c mice in conjunction with intravenous administration of DOXIL® [[Doxil]] (dosed in a range of 2, 10, or 20 mg/kg), a liposomal preparation of doxorubicin, to mice enhanced AV2FLAG-luc transduction by 2 logs by day 7 at the 20 mk/kg dose of DOXIL® [[doxil]]. Specifically, at 20 mg/kg DOXIL® [[doxil]], transduction was enhanced on the average of 67-fold by day 7 and 4-fold by day 30. It is worth noting that DOXIL® [[doxil]] previously tested negative in cell line screening while the free compound doxorubicin tested positive in cell line screening (Figures 1A-E). Liposomal formulations have desirable properties for *in vivo* use including their increased stability or circulation half life making them more bioavailable *in vivo*. Those same characteristics make liposomal formulations less desirable for *in vitro* screening as described

above. Thus, one skilled in the art can design formulation strategies for agents of the invention to tailor them to the desired application. In addition to formulation design, one skilled in the art can tailor routes of delivery in order to maximize rAAV transduction efficiencies.

Please amend the paragraph beginning on page 82, line 12 as follows:

In additional experiments, a pseudotyped rAAV vector encoding FVIII was tested in male Rag-1 mice. Rag-1 mice were used because as described in the art, normal mice produce inhibitors of human FVIII that can obscure protein detection in the serum. Rag-1 mice are known to be deficient in the pathways necessary to produce these inhibitors and thus will either produce no inhibitors, lower levels of inhibitors or have extended time periods for development of inhibitors. The rAAV vector was constructed containing serotype 5 capsid proteins and 5'-3' ITRs of AAV-2 flanking a heterologous transgene comprised of the minimal liver specific element HNF3/EBP and a human B-domain deleted FVIII gene (a second construct was identical except it contained a B-domain deleted canine FVIII gene). Animals were administered 10^{12} rAAV vector particles intravenously via the lateral teil vein concurrently with 20 mg/kg of DOXIL® [[doxil]] at day 0. Circulating, bioavailable FVIII activity was measured from the serum at days 31, 53 and 90 by techniques known in the art including ELISA and Coatest. Data presented in Figure 3 demonstrate that animals not treated with DOXIL® [[doxil]] had barely detectable levels of FVIII in the range of 0.99 ng/ml for days 31 and 53 which decreased to 0.13 ng/ml by day 90. In contrast, animals dosed with 20 mg/kg of DOXIL® [[doxil]] had over 40 times the levels of FVIII protein. Interestingly, the decline in FVIII protein seen in animals not treated with DOXIL® [[doxil]] at day 90 (0.13 ng/ml) was not evident in animals treated with DOXIL® [[doxil]] (40.16 ng/ml) indicating that DOXIL® [[doxil]] not only enhanced rAAV transduction as evident at the shorter time period, but the agent of the invention also prolonged expression. In order to demonstrate that DOXIL® [[doxil]] was affecting rAAV transduction and not merely affecting the FVIII protein translation or stability, RS-PCR was performed on liver tissue at the day 53 time point. The data presented for individual animals in Table 1 demonstrates that the increase in FVIII protein noted in animals treated with DOXIL® [[doxil]] correlates with the levels of mRNA detected.

Please amend the paragraph beginning on page 83, line 7 as follows:

The increase *in vivo* rAAV transduction produced by DOXIL® [[doxil]] was further confirmed utilizing the same vectors and protocol described above in male FVIII knockout mice tolerized to the human FVIII protein utilizing a cytoxan mediated tolerization strategy as described in the art. Animals were treated with weekly injection of 50 mg/kg cytoxan beginning at the time of rAAV vector delivery. Data presented in Table 2 confirmed the previously described results when tested by ELISA or Coatest at days 14 and 25, namely animals dosed with DOXIL® [[doxil]] demonstrated at least a ten-fold enhancement of rAAV transduction.

Please amend the paragraph beginning on page 110, line 14 as follows:

Intranasal administration of doxorubicin and idamycin at 10% HDE were both associated with early mortality of some animals, ruffled hair coats and sick mice. In addition, those animals that survived also lost considerable body weight over the week. The intranasally DOXIL® [[doxil]] treated mice did better than the doxorubicin- or idamycin-treated animals in that there was no early mortality and they appeared clinically normal. However, they also lost weight. The intravenously DOXIL® [[doxil]] treated mice fared the best.

Please amend the paragraph beginning on page 110, line 21 as follows:

Intranasal treatment of doxorubicin and idamycin resulted in increased luciferase expression (Figure 21 and Table 6). Treatment with DOXIL® [[doxil]] at a 10% HDE (both intravenously and intranasally) resulted in an average increase in luciferase expression by 49- and 74-fold, respectively, 7 days post-dose.